Unveiling amyloid-β1–42 interaction with zinc in water and mixed hexafluoroisopropanol solution in Alzheimer's disease

ABSTRACT

Alzheimer's disease (AD) is a neurodegenerative disorder caused by overproduction and accumulation of amyloid beta-peptide (Aβ). The hallmarks associated with this AD are the presence of Aβ plaques between the nerve cell in the brain which leading to synaptic loss in memory. The amyloid plaques contain of transition metals like zinc, copper and iron. In a healthy brain, the metal ions are present in balance concentration. High concentrations of Zn are normally released during neurotransmission process. The release of Zn might cause the aggregation of Aβ leading to AD. Amyloid-β1–42 is the main type of Aβ in amyloid plaque. There still have limited explanation on how Aβ1–42 interaction with Zn metal, as well as the effect of Zn metal on the Aβ structure in different solvents in atomic detail. Therefore, we investigated the structural changes of Aβ1–42 in water (Aβ-H2O) and the mixed hexafluoroisopropanol (HFIP) with water (Aβ-HFIP/H2O). The mixed solvent consisted of hexafluoroisopropanol (HFIP) and water was used with the ratio of HFIP:H2O (80:20). The effect of zinc ion was also examined for the interaction of Aβ peptide with zinc in water (Aβ-Zn-H2O) and mixed solvent (Aβ-Zn-HFIP/H2O) using all atom level molecular dynamics (MD) calculations for 1 μs. We found that Aβ-Zn-HFIP/H2O contained more α-helix compared to Aβ-HFIP/H2O while Aβ-H2O and Aβ-Zn-H2O produced well-dissolved structure and they contained more β-sheets. β-turns are possible to bind with the receptor proteins and may induce the aggregation process in AD. Thus, Aβ-H2O and Aβ-Zn-H2O have higher possibility leading to AD compared to Aβ-Zn-HFIP/H2O and Aβ-HFIP/H2O models.

Keyword: Amyloid-β1–42; Alzheimer disease; Hexafluoroisopropanol (HFIP); Molecular dynamics simulation